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| APPLICATION NO. | FILING DATE | FIRST NAMED INVENTOR | ATTORNEY DOCKET NO. | CONFIRMATION NO. |
|---|-------------|----------------------|------------------------|------------------|
| 10/632,567 | 07/31/2003 | Paul Workman | CCI-026US | 2601 |
| 959 | 7590 | 06/22/2006 | EXAMINER | |
| LAHIVE & COCKFIELD 28 STATE STREET BOSTON, MA 02109 | | | PERREIRA, MELISSA JEAN | |
| | | | ART UNIT | PAPER NUMBER |
| | | | 1618 | |

DATE MAILED: 06/22/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.

10/632,567

Applicant(s)

WORKMAN ET AL.

Examiner

Melissa Perreira

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 31 July 2003.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-18,22-25,27 and 28 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 1-18,22-25,27 and 28 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☒ The drawing(s) filed on 31 July 2003 is/are: a) ☒ accepted or b) ☐ objected to by the Examiner.
- Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
- Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☒ None of:
1. ☒ Certified copies of the priority documents have been received.
 2. ☐ Certified copies of the priority documents have been received in Application No. _____.
 3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|---|---|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413) |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | Paper No(s)/Mail Date. _____ |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) | 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152) |
| Paper No(s)/Mail Date _____ | 6) <input type="checkbox"/> Other: _____ |

DETAILED ACTION

1. The title of the invention is not descriptive. A new title is required that is clearly indicative of the invention to which the claims are directed.
2. Acknowledgment is made of applicant's claim for foreign priority based on an application filed in United Kingdom on January 31, 2001. It is noted, however, that applicant has not filed a certified copy of the patent application as required by 35 U.S.C. 119(b).

Claim Rejections - 35 USC § 103

3. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

4. Claims 1-18,22-25,27 and 28 are rejected under 35 U.S.C. 103(a) as being unpatentable over Dumont et al. (US 6,413,974) in view of the combined teachings of Dumont et al. (US 6,399,633) and Carlson et al. (*Cancer Res.* **1999**, 59, 4634-4641).
5. Dumont et al. (US 6,413,974) teaches the co-administration, not excluding a human of more than one cyclin dependent kinase inhibitor (cassette dosing assay) in a therapeutically effective amount (column 42, lines 32-36; column 44, lines 52-54). The cyclin dependent kinase inhibitor roscovitine has been shown to be selective towards some cyclin-dependent kinases where none of the analogs showed superior IC₅₀ values over the (R) enantiomer of roscovitine (column 13, lines 28-50). Roscovitine was tested

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against the human colon adenocarcinoma cell lines HT-29 and HCT-15 (table 1) and in *in vivo* assays where nude mice xenografts where tumor pieces were implanted under the capsule of the kidneys of male nude mice (column 101, lines 5-21). Dumont et al. (US 6,413,974) does not teach the monitoring of the phosphorylation of ERK1/2, phosphorylation of Rb at serine 780 or the antibodies necessary to monitor these phosphorylations.

6. Dumont et al. (US 6,399,633) discloses the administration of cyclin dependent kinase inhibitor flavopiridol over 3 days and the study of its effects on phosphorylated pRb and levels of phosphorylated ERK1 and ERK2 using the specific antibodies that recognize pRb and phosphorylated ERK1/2 (Fig 2., column 2, lines 58-67; column 3, lines 1-8). The percentage of viable cells was examined up to 24 r and the dosage requirements were examined in nude mouse xenograft models (Fig. 6, column 6, lines 53-63), not excluding KM12 colon cancer cells. Phosphorylation of Rb was inhibited by the use of flavopiridol and the phosphorylation of ERK1/2 was not blocked by the use of flavopiridol (column 13, lines 30-33; column 10, lines 9-50).

7. Carlson et al. (*Cancer Res.* **1999**, 59, 4634-4641) discloses the specific polyclonal antisera that recognizes the phosphorylated serine 780 Rb species to determine the mechanism by which flavopiridol, a cyclin dependent kinase inhibitor, inhibits cyclin D1 abundance in breast carcinoma cells (p 4634, column 2, paragraph 4) thus causing dephosphorylation of pRb. Minimal changes (upto 8 h) were observed in the phosphorylated Rb at serine 780 or in total Rb but Rb phosphorylation declined at 12 h after treatment with flavopiridol (p 4636, paragraph 2).

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8. At the time of invention for one ordinarily skilled in the art to use the teachings of Dumont et al. (US 6,399,633) that 4-H-1-benzopyran-4-one derivatives are suitable for controlling tumor growth (column 2, lines 17-18) and utilize (R)-roscovitine, taught by Dumont et al. (US 6,413,974), a selective and a more potent cyclin dependent kinase inhibitor to study its effects on serine 780 Rb phosphorylation of Rb and levels of phosphorylated ERK1 and ERK2 using the specific antibodies for pRb and ERK1/2.

Conclusion

No claims are allowed at this time.

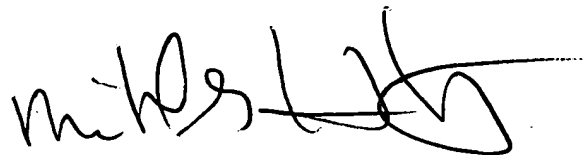
Any inquiry concerning this communication or earlier communications from the examiner should be directed to Melissa Perreira whose telephone number is 571-272-1354. The examiner can normally be reached on 9am-5pm M-F.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Mike Hartley can be reached on 571-272-0616. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

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Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

MP
May 31, 2006

A handwritten signature in black ink, appearing to read 'Michael G. Hartley', with a stylized flourish at the end.

MICHAEL G. HARTLEY
SUPERVISORY PATENT EXAMINER